Express Mail No. EV 327053773 US

REMARKS

Specification

The abstract of the disclosure was objected to because of inclusion of the word "comprising" therein. Applicants submit herewith an amended version of the abstract, wherein the word "comprising" has been replaced with "containing."

The disclosure was objected to because of the embedded hyperlink present on page 23, line 6. The hyperlink has been deleted. Furthermore, the specification has been reviewed and no other hyperlinks were found.

The specification was objected to because it failed to provide proper antecedent basis for the claimed subject matter, in particular for oligonucleotide sequence GCA GNN $(NNN)_7$. Applicants respectfully disagree. The antecedent basis for GCA GNN $(NNN)_7$ is provided on page 11, lines 23-27.

Applicants have reviewed the application for presence of minor errors, and have corrected them. The corrections can be found in *Amendments to the Specification*, pages 2-4.

Rejection Pursuant to 35 U.S.C. § 112, 1st ¶

Reconsideration is requested of the rejection of claims 1-9 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

According to the Office, the specification failed to provide an adequate written description of the method for identifying a non-Ig peptide with an affinity for the surface of ***any*** kind of fungi (emphasis added). Furthermore, the Office noted that Bishop-Hurley (Phytopathology, page S7) discloses that the effect induced by a peptide on fungi was species-specific.

Applicants note that the claim 1 is not directed to a method for identifying non-Ig peptides with an affinity for the surface of any kind of fungi; rather, claim 1 is directed to a method for identifying non-Ig peptides that have an affinity for the surface of **a fungus**.

As a further note, claim 1 requires testing random peptide libraries for their ability to bind to a fungus. The peptide or peptides that bind to that particular fungus are then selected and identified. The claim, however, does not require that the peptides have affinity for all, or even another fungus. In general, the method of claim 1 is applicable to many different fungi, and thus, non-Ig peptides that bind to a number of fungi can be identified; however, the random peptide libraries are not tested to select peptides that bind to multiple fungi.

The species-specific effect of peptides on a fungus was described by Bishop-Hurley, as mentioned in the Office action. The same species-specific effect can also be seen in Example 6 (page 24, lines 8-14), where it is indicated that phage-bearing peptides selected for *P. capsici* showed no or little encystment when incubated with *P. sojae* or *P. parastica*. Applicants believe that this further demonstrates their point that non-immunoglobulin peptides selected by the method of claim 1 show specificity and selectivity for a particular fungus. In addition, by utilizing a different fungus in the present method, one can select non-immunoglobulin peptides that bind specifically to that fungus, thus allowing for identification of non-immunoglobulin peptides that have affinities for a large number of fungi.

Rejection Pursuant to 35 U.S.C. § 112, 2nd ¶

Reconsideration is requested of the rejection of claims 1-9 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

According to the Office, the word "capable" in claim 1 connotes uncertainty, i.e., whether the host has been positively transfected by the fusion vector. Applicants respectfully disagree.

Claim 1 merely requires that the vector express a library of peptides on the surface and that it be compatible with a host cell, i.e., that it can transfect a host cell. Stated another way, a number of different vectors that express peptides on the surface and transfect host cells may be used. A skilled artisan can readily determine whether a particular vector may be used for the purposes of the present invention based on its

ability to transfect a particular host cell. Applicants further note that a brief search of USPTO database yielded 407 results for patents that recite "vector capable of" in the claims.

Applicants have amended claim 8, wherein the word "estimating" has been replaced with the word "determining". Support for determining binding affinity and how such affinity is determined can be found, e.g., at page 13, lines 35-36, and page 14, lines 1-8. Both competitive binding and Scatchard analysis that are described on page 13 are well known in the art.

Claim 9 has been amended to reflect the fact that each of the peptides are of the same length, which is from 6 to 15 residues. Each peptide library generally contains peptides of same length, but peptides in different libraries can generally vary in length from about 6 to about 15 amino acids long. For example, as stated in the specification, f8-1 library utilizes random 8-mer peptides (page 11, lines 12-14), and f88-4 utilizes random 15-mer peptides (page 11, lines 14-15). Claim 9 has been amended to more accurately describe peptide length.

Rejection Pursuant to 35 U.S.C. § 103

Reconsideration is requested of the rejection of claims 1-9 under 35 U.S.C. § 103(a) as being unpatentable over Gyuris *et al.* (U.S. Patent No. 6,420,110) or Massey (WO 99/51780).

Claim 1 relates to a method for idenitfying non-immunoglobulin peptides that have an affinity for the surface of a fungus. The method includes the following steps: 1) constructing a library of peptides, 2) contacting a vector expressing said library with a target fungus and removing unbound vector; 3) eluting bound vector from the fungus, 4) amplifying bound vector, 5) sequencing oligonucleotides contained in said vector, 6) deducing the amino acid sequence of peptides encoded by said oligonucleotides, and 7) selecting the non-immunoglobulin peptides. The library of step (1) is created by: a) preparing random oligonucleotides, b) inserting the oligonucleotides into a vector that expresses peptides encoded by said random oligonucleotides on its surface and is capable of transfecting a host cell, and c) transfecting a host cell with the vector to

amplify the vector in an infectious form to create a library of peptides on the surface of the vector.

Guyris *et al.* describe a method of generating a peptide with a selected biological activity. Guyris et al.'s method comprises (a) providing a recombinant host cell population which expresses a **soluble** peptide library comprising a variegated population of test peptides, (b) culturing the host cells with a target microorganism (bacteria or fungus) under conditions wherein the peptide library is **secreted** and **diffuses** to the target microorganism; and (c) selecting host cells expressing test peptides that inhibit growth of the target microorganism. (Guyris et al., at column 4, lines 25-35, emphasis added).

There are numerous differences between the requirements of claim 1 and the method disclosed by Guyris et al. Claim 1 requires the expression of the library of peptides on the surface of a vector to test for their ability to bind to a target fungus whereas Guyris *et al.*'s method requires the **secretion** of peptides which are **free of the display packages**. Claim 1 is directed to a method for the identification of non-immunoglobulin peptides whereas Guyris et al. are merely concerned with peptides having antimicrobial activity. Thus, Guyris et al. do not disclose contacting a vector which expresses peptides on its surface with fungus, eluting unbound vector from said fungus, amplifying the bound vector, sequencing the oligonucleotides contained in the eluted vector, deducing the amino acid sequence of peptides encoded by the vecotr and selcing the non-immunoglobulin peptides, all as required by claim 1.

Significantly, the peptides of claim 1 are directly fused to a surface protein of a vector, i.e., oligonucleotides that encode these peptides are inserted into the oligonucleotide sequence of one of the vector surface proteins, and are thus expressed as parts of such surface proteins. In contrast, each of Guyris *et al.*'s peptides are encoded by a chimeric gene, which contains a coding sequence of the test peptide, a coding sequence for a surface protein of the display package, and RNA splice sites flanking the coding sequence for the surface protein, such that the test peptide is expressed without the surface protein as a result of the coding sequence for the surface protein being removed by RNA splicing (i.e., the test peptide is secreted).

The method of claim 1 is based on binding of vector-displayed peptides to a target fungus; thus, it involves a direct contact of a fungus with the vector-displayed peptides. This is in contrast to the method of Guyris et al., which is based on co-cultivation of a target microorganism and host cells that secrete soluble peptides. Accordingly, Guyris *et al.* teach away from the claimed invention by requiring that 1) a peptide be tested free from its display package; 2) a peptide be tested in secreted form; and 3) a chimeric gene containing a coding sequence of a test peptide and a coding sequence of a surface protein of a display package also include RNA splice sites.

According to the Office, one skilled in the art would have been motivated to choose a fungus as a microorganism as taught by Guyris *et al.* Guyris et al. disclose that a target microorganism can be a bacteria or a fungus. In such cases, host cells (that secrete peptides) are cultured on agar embedded with a target microorganism, and antimicrobial activity of a test peptide is determined by zone clearing in the agar. Even if a skilled artisan would have been motivated to choose a fungus as a microorganism in Guyris *et al.* method, however, this would not have produced the invention defined by claim 1.

Massey *et al.* disclose a method for inhibiting growth of a target cell or target tissue, wherein said target cell or target tissue is distinguished from normal cells or normal tissue in at least one surface component. Massey *et al.* provide a method of selecting one or more peptides or protein bound to a carrier, wherein the peptide(s) or protein bind to epitopes expressed on one target class of cells or tissue only. These proteins or peptides with their carriers are then used to identify desired target cells or target tissue *in situ*. Following administration of at least one member of the selected peptide or protein expression library to an animal or human, the immune system targets a desired cell for elimination by "decorating" the target cell with the carrier bearing a peptide, which specifically binds to the target cell. The peptide expression library, as described by Massey *et al.*, utilizes peptides that are covalently attached to a carrier in order to be able to elicit an immune response against said carrier in a human or animal. By creating an immune response against a carrier, an immune response is also created against the peptide that is covalently bound to said carrier, thereby mediating killing,

inhibition or removal of a target cell. Furthermore, it is stated on page 5, lines 28-31 of Massey *et al.* that "it is a *crucial* aspect of the present methods that the carrier on which the peptide expression library is expressed is itself recognized as immunogenic by the animal or human in which use is sought" (emphasis added).

As discussed above, the method of claim 1 identifies non-immunoglobulin peptides that have the ability to bind to a target fungus. This method is useful for identifying peptides that bind to pathogenic fungi, particularly where the fungi are of the genus *Phytophthora*. Thus, whereas in the method of claim 1, a target organism is a fungus, in Massey *et al.*, a target cell is a tumor cell, or a virus-, pathogen-, or protozoan-infected cell (see, e.g., page 3, lines 29-31). Furthermore, the peptides identified by the method of claim 1 are encoded by random oligonucleotides expressed by a vector, which is capable of expressing said peptides on its surface and transfecting a host cell. In contrast, Massey *et al.* require that the peptide expression library be expressed on an immunogenic carrier in order to be able to generate an immunological response against the target cell. In addition, the antifungal peptides identified by the method of claim 1 inhibit fungal growth/proliferation by a direct interaction, whereas in Massey *et al.*, the inhibition or removal of the target cell occurs *through an immunological response*. Accordingly, based on the above-mentioned differences, Applicants submit that Massey *et al.* teach away from the claimed invention.

When considered in combination, Guyris *et al.* and Massey *et al.* would not have led a person of ordinary skill to the claimed invention. Guyris et al.'s method requires identifying a peptide with a selected biological activity by expressing the peptide in a co-culture in free and secreted form, contrary to the requirements of claim 1. Similarly, Massey et al. disclose a method for inhibiting growth of a target cell by creating an immune response against the target cell, contrary to the requirements of claim 1.

Claims 2-9 depend from claim 1 and introduce additional requirements. They are patentable over the combined disclosure of Guyris et al. and Massey et al. for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

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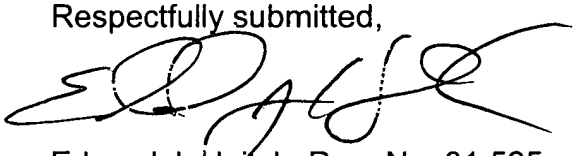
CONCLUSION

In view of the above, Applicants respectfully request favorable reconsideration and allowance of the pending claims.

Enclosed is applicants' check in the amount of $55.00 for payment of the surcharge, filing fee and one month extension of time. The Commissioner is hereby authorized to charge any deficiency or overpayment of the required fee to Deposit Account No. 19-1345.

Respectfully submitted,



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